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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/814,604 | 03/22/2001 | Elliott S. Klein | P-AR 4528 | 4120 |

23601 7590 12/02/2002

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EXAMINER

MURPHY, JOSEPH F

ART UNIT

PAPER NUMBER

1646

DATE MAILED: 12/02/2002

10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicant(s) N .

09/814,604

Applicant(s)

KLEIN ET AL.

Examiner

Joseph F Murphy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 September 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of the Species RAR and the Species TIF-2/GRIP-1/NcoA-2 in Paper No. 9, 9/23/2002 is acknowledged. The traversal is on the ground(s) that there is no burden to search all the species. This is not found persuasive because a search is directed to references which would render the invention obvious, as well as references directed to anticipation of the invention, and therefore requires a search of relevant literature in many different areas of subject matter.

The requirement is still deemed proper and is therefore made FINAL.

The search has been broadened to include the species of coactivator SRC-1/NcoA-1.

Claim 15 will thus be examined. Claims 1-26 are pending and under consideration.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-26 rejected under 35 U.S.C. 102(a) as being anticipated by Klein et al. (2000).

Klein et al. teaches the repression of the transcriptional activity of a constitutively active RARgamma-VP-16 chimeric receptor by the inverse agonist AGN193109 requires a functional Co-R box and that binding of this ligand to RARgamma leads to an increased interaction with

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the corepressor N-CoR both in glutathione S-transferase pull-down and yeast two-hybrid analyses (page 19401). Klein et al. teaches that under conditions which favor ternary complex formation, a RAR neutral antagonist is distinguished from an inverse agonist with respect to corepressor recruitment as is a RAR partial agonist distinguished from an agonist with respect to coactivator recruitment. The method by which corepressor recruitment and coactivator recruitment is determined is set forth on page 19405, Figure 4. In this assay, the agents 193109 and 193840 were contacted to a nuclear hormone receptor (RAR)-RXR heterodimers) and the coactivator and corepressor association was measured (Figure 4 A and B). Thus claims 1-26 are anticipated.

Claims 1-26 are rejected under 35 U.S.C. 102(b) as being anticipated by DiRenzo et al. (1997).

Direnzo et al. describes allosteric interactions between RXR and two heterodimeric partners, retinoic acid receptors (RARs) and peroxisome proliferator-activated receptors (PPARs); RARs and PPARs prevent and permit activation by RXR-specific ligands, respectively (page 2166). Durenzo et al. teaches a method of determining the effect of an agent (TTNPB) on the recruitment of corepressor (NCoR) and coactivator (SRC-1) on RAR and PPAR (page 2173, Figure 6). In this method both the coactivator and corepressor are measured. This anticipates claims 1-26.

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over DiRenzo et al. (1997).

DiRenzo et al. describes allosteric interactions between RXR and two heterodimeric partners, retinoic acid receptors (RARs) and peroxisome proliferator-activated receptors (PPARs); RARs and PPARs prevent and permit activation by RXR-specific ligands, respectively (page 2166). DiRenzo et al. teaches a method of determining the effect of an agent (TTNPB) on the recruitment of corepressor (NCoR) and coactivator (SRC-1) on RAR and PPAR (page 2173, Figure 6). In this method both the coactivator and corepressor are measured. DiRenzo et al. further discloses that it is possible that other members of the SRC-1 family of coactivators, such as TIF-2 are also coactivators for nuclear hormone receptors (page 2175 column 1, first

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paragraph). Therefore it would have been obvious to one of skill in the art at the time the invention was made to practice a method of method of determining the effect of an agent on the recruitment of corepressor and coactivator (wherein the coactivator is TIF-2/GRIP-1/NcoA-2) on RAR. The motivation is provided in DiRenzo et al. who teaches that arriving at an understanding of the mechanisms by which coactivators and corepressors function and characterizing their biological roles will be of great interest (page 2175, column 1, fourth paragraph).

Conclusion

No claim is allowed.

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Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245.

The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
November 27, 2002